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REPUBLIC OF THE PHILIPPINES DURING 1976-1977

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Influenza Surveillance in Manila, Republic of the Philippines During 1976-1977

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INTRODUCTION

The recent emergence of A/USSR/77 (H1N1) virus¹ once again demonstrates that new strains of influenza A virus often originate in Southeast Asia during the early summer months, migrate to other areas of the world and become epidemic or occasionally pandemic.² For this reason, U.S. Naval Medical Research Unit No. 2 (NAMRU-2) Taipei, Taiwan, has maintained an active surveillance program for influenza in the Western Pacific including the Philippines.

Several periods of influenza activity have occurred in Manila during 1976 and 1977. The isolates recovered during this period cover a broad spectrum of antigenic strains.

MATERIALS AND METHODS

Sample Population. Febrile patients at San Lazaro Hospital who had clinical signs and symptoms compatible with influenza were selected for virus isolation and serology studies. The majority of patients entering the study were from Metropolitan Manila.

Virus Isolation and Identification. Those patients who had onsets three days or less prior to reporting to the outpatient services were selected for virus isolation attempts.

Cotton applications were used to swab the oropharynx of selected patients and the swabs were then immersed in a one dram vial containing 2.5 ml brain heart infusion broth having a final concentration of 200 units of penicillin/ml and 200 ug of streptomycin/ml. The vials containing the swabs were sealed with paraffin film and placed in a mechanical freezer at -80°C and air transported on dry ice to NAMRU-2 in Taipei.

In 1976, virus isolation was attempted in both 10-11 day old chicken embryos (CE) and, in most in-

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stances, monolayers of primary monkey kidney cells. In 1977, CE and monolayers of a continuous line of canine kidney (MDCK) cells were used for isolation. Hemagglutinating (HA) agents isolated were identified by standard hemagglutination inhibition (HAI) procedures¹. Reference HA antigens and antisera used in identification of isolates were supplied by the World Health Organization (WHO) Collaborating Center for Influenza Viruses, Center for Disease Control, Atlanta, Georgia, U.S.A. Selected isolates were sent to the WHO Collaborating Center for confirmation of identification.

Serologic Studies. Acute phase venous blood specimens were taken at the same time as throat swabs and also from patients whose onset had been greater than three days before presentation at the outpatient clinic.

Convalescent bloods were drawn from as many patients as possible after an interval of 14 days or more from the time of onset. After clotting, all blood samples were centrifuged and the serum transferred to screw capped vials and stored at -20°C until they were transported on dry ice to NAMRU-2 for testing.

Tests for HAI antibodies to influenza viruses were performed using standard techniques¹ using reference HA antigens and control sera supplied by the WHO Collaborating Center. The HA antigens used were A/Victoria/75 (H3N2), A/New Jersey (NJ)/76 (H1N1), B/HK/72 and A/USSR/77 (H1N1). Sera were tested against A/USSR/

77 antigen only after October 1977 and testing for A/NJ/76 HAI antibodies was discontinued in 1977. Dengue HAI tests were also performed using standard techniques¹ using kaolin absorbed sera and prototype DEN-1 and DEN-2 sucrose-acetone extracted suckling mouse brain antigens. Criterion for serologic evidence of recent infection was a four-fold or greater rise in HAI antibody titer.

RESULTS

Virus Isolation. The distribution of isolates during 1976 is presented in Table I. Virus was isolated in 8 months of the year. All strains isolated during the period were of the H3N2 subtype but were of two antigenically distinguishable strains: A/Victoria/75-like and A/Texas/77-like. These two strains are cross-reactive in HAI tests but are nonetheless distinguishable. The A/Texas/77-like strains were first isolated by us in Manila in August 1976.

The distribution of isolates in 1977 is presented in Table II. Fewer strains were isolated during 1977 but fewer attempts at isolation were made. The isolation of strains was again scattered throughout the year. However, in 1977 the situation was more complex than 1976: both type A and type B isolates were made and, furthermore, two subtypes of type A, H3N2 and H1N1 were isolated. The presence of two type A influenza subtypes was further complicated by the H3N2 strains being of two distinguishable strains, A/Victoria/75-like and A/Texas/77-like.

TABLE 1
ISOLATION OF INFLUENZA VIRUS BY MONTH, MANILA, 1976

Virus Identification	Month Samples Taken for Isolation												Year's Total
	Jan (67)*	Feb (37)	Mar (33)	Apr (16)	May (19)	Jun (27)	Jul (12)	Aug (30)	Sep (18)	Oct (10)	Nov (8)	Dec (8)	
A/VIC/75 or A/TEL/77 (H1N2)	4	1	6	3	6	3	1	7	2	0	0	0	27
B/TEL/72	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	4	1	6	3	6	3	1	7	2	0	0	0	27

* () = Number of isolations attempted.

TABLE II
ISOLATIONS OF INFLUENZA VIRUS BY MONTH, MANILA, 1977

Virus Identification	Month Samples Taken for Isolation												Year's Total
	Jan (3)*	Feb (5)	Mar (10)	Apr (14)	May (6)	Jun (13)	Jul (6)	Aug (9)	Sep (4)	Oct (17)	Nov (19)	Dec (15)	
A/VIC/75 or A/TEX/77 (H2N2)	0	0	2	0	0	3	0	0	0	0	0	0	10
B/HK/72	0	0	0	0	2	1	0	0	0	0	0	0	3
A/US62/77 (H1N1)	0	0	0	0	0	0	0	0	0	0	1	1	2
Total	0	0	2	0	2	9	0	0	0	0	1	1	15

* () = Number of isolations attempted.

Temporarily, the 1977 strains were distributed as follows: the 2 H3N2 strains isolated in March were both A/Victoria/75-like. The 8 H3N2 strains isolated in June were all A/Texas/77-like. Three strains of type B influenza similar to B/Hon Kong/73 were isolated in May and June. The newly emergent or re-emergent¹ H1N1 strain was isolated in November and December and the isolates were A/USSR/77-like.

Serology. During 1976, 87 paired sera were examined using A/Victoria/75, A/New Jersey/76, and B/Hong Kong/73 HA antigens (Table III). Of these, 18 showed four-fold rises in HAI antibody titer. Paired

sera were not obtained in a uniform manner month by month throughout the year. (Table III).

In 1977, 73 paired sera were tested for HAI antibodies. From January to October, only tests for A/Victoria/75 and B/Hong Kong/73 HAI antibody were made. After October all paired sera were also tested for A/USSR/77 HAI antibodies. The results of the serological tests are presented in Table IV.

Additionally, in 1977, 24 pairs of sera were tested against DEN-1 and DEN-2 HA antigens. Nine of these 24 paired sera showed a 4-fold or greater rise in HAI antibody titer from acute to convalescent serum samples.

TABLE III
RESULTS OF INFLUENZA HAI TESTS ON PAIRED PATIENT SERA,
MANILA, 1976

Test Results	Antigen		
	A/VIC/75 (H3N2)	A/NJ/76 (H1N1)	B/HK/73
Positive*	18**	1+	10
Negative	71	86	86
Total	87	87	87

* Four-fold or greater rise from acute to convalescent serum specimens.

** Number of patients positive by month of onset: 5 in June, 10 in Aug. one in October.

+ Onset occurred during August.

@ Onset occurred during October.

TABLE IV
RESULTS OF INFLUENZA AND DENGUE HAI TESTS ON PAIRED
PATIENT SERA, 1977, MANILA

Test Results	Antigen			
	A/VIC/75	A/USSR/77	B/HK/72	DEN-1 & DEN-2
Positive**	1*	5*	0	9@
Negative	70	42	72	13
Total	72	47	72	24

* Four-fold or greater rise from acute to convalescent serum specimens.

** Patient's onset was in September

* Number of patients positive by month of onset: October, 2, December, 3.

@ Number of patients positive by month of onset: April, 1, June, 1; July, 1; August, 3; September, 1; October, 1, November, 1.

DISCUSSION

Influenza strains were seen in Manila after they had been seen elsewhere in the Western Pacific region. Specifically, in 1976, a strain of H3N2 influenza was isolated in August. This strain resembled a virus isolated earlier that same summer in Australia, A/Victoria/76 (H3N2). Both the Manila isolate and the Australian isolate closely resemble a strain which was subsequently isolated in Texas in January 1977, A/TEX/77 (H3N2). A/TEX/77, in later months, became a cause of epidemic disease in the U.S.^{1*}

Again in 1977 a new strain of influenza, this time a new or recurrent subtype, H1N1, was isolated in November. This isolated closely resembled others which had caused epidemic disease in the Soviet Union and Hong Kong in October¹. Similar strains had apparently been circulating in China as early as May of 1977¹. This virus was later implicated as a cause of epidemic disease in the U.S. and Western Europe¹. The isolation of these strains of influenza and one previously reported² at an early time in Manila stress the importance of this type of surveillance from both a regional and a global view.

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Manila continues to experience outbreaks of influenza due to a variety of influenza strains. The temporal distribution of isolates during this two year study demonstrates that influenza virus can occur at any time of the year in Manila as opposed to the generally held concept of a "flu season" which occurs in more temperate climates.

Although no data on school absenteeism or excess mortality due to respiratory disease were collected during this study, no serious epidemic of influenza seems to have occurred during the reporting period. This can be partially explained by A/VIC/75 and A/TEX/77 being variants within the H3N2 subtype — a subtype to which most persons possess antibodies. This herd immunity effect tends to limit the extent of outbreaks among the general population and also the severity of disease among individuals who possess such antibody². Also the A/USSR/77-like viruses which were isolated in Manila are very similar to A/FM/46 (H1N1)⁶. This similarity leads to a similar herd immunity phenomenon but only in persons that were born prior to or during the last H1N1 era. Thus, persons born after 1957 would be immunologically naive to H1N1 viruses and, therefore, if the viruses are sufficiently similar, only those

persons not previously exposed would be expected to experience disease. Although only two isolates were made, both were from persons of less than 5 years of age. This age distribution with A/USSR/77-like viruses has also been found in other NAMRU-2 studies^{10,11} and in outbreaks in the Western Hemisphere⁸.

Difficulties in obtaining paired sera have made this portion of the surveillance program less than ideal. Nevertheless, serologic rises generally confirm what isolation data has already demonstrated: several strains of influenza virus have been active and they are responsible for febrile illness.

The presence of rising HAI antibody titers to both dengue and influenza viruses among our study population indicates the non-specific nature of dengue and influenza and the difficulty in making clinical diagnoses of a definitive nature without adequate laboratory support. Although the number of sera tested were small, the higher proportion of paired sera in which 4-fold or greater dengue HAI antibody titer rises occurred may indicate that mild dengue fever was a more frequent cause of febrile illness than influenza during 1977 in the patients of San Lazaro Hospital.

SUMMARY

Influenza surveillance was performed among patients admitted at San Lazaro Hospital in Manila from January 1976 to December 1977. Twenty-seven influenza strains were isolated in 1976 and 16 in 1977. The 1976 strains were all of the H3N2 subtype although some were similar to A/Victoria/75 (H3N2) and others to A/Texas/77 (H3N2). The 1977 influenza isolates were more diverse: Two subtypes of type A influenza were isolated, H3N2 (as

in 1976) and a H1N1 virus similar to A/USSR/77 was first isolated in November 1977. Type B influenza was also isolated from three patients in May and June 1977.

Serologic tests on paired patient sera confirmed the virus isolation findings. In addition, several persons admitted to the influenza study had rising HI antibody titers to DEN-1 and DEN-2 antigens, indicating that the probable cause of their febrile illnesses was dengue virus.

REFERENCES

1. U.S. Dept. HEW, PHS, CDC. Morbidity and Mortality Weekly Report 26:410, 1977.
2. Kilbourne, E.D. Epidemiology of Influenza. In *The Influenza Viruses and Influenza*. Kilbourne, E.D., editor. Academic Press Inc., New York, 1975.
3. U.S. Dept. HEW, PHS. Advanced Laboratory Techniques for Influenza Diagnosis. USPHS, Atlanta, Immunology Series No. 6, Procedural Guide, 1975.
4. Hanmon, W.McD. and Sather, G.E. Arboviruses. In *Diagnostic Procedures for Viral and Rickettsial Infections*. Lenette, E.H. and Schmidt, N.J., editors. American Public Health Association, Inc., New York, 1968.
5. U.S. Dept. HEW, PHS, CDC. Morbidity and Mortality Weekly Report 26:444, 1977.
6. U.S. Dept. HEW, PHS, CDC. Morbidity and Mortality Weekly Report 27:16, 1978.
7. U.S. Dept. HEW, PHS, CDC. Morbidity and Mortality Weekly Report 27:24, 1978.
8. U.S. Dept. HEW, PHS, CDC. Morbidity and Mortality Weekly Report 27:64, 1978.
9. Olson, J.O., Rodriguez, T.O., Irving, G.B. and Uylangco, G.V. Influenza surveillance in Manila, Republic of the Philippines during 1978. *Philippine J. Microbiol. Infec. Dis.* 2:9-16, 1978.
10. Olson, J.O., Kalazek, T.O., Irving, G.B. and Rendin, R.M. An explosive outbreak of influenza caused by A/USSR/77-like virus on a U.S. Naval Ship. *Military Med.* (In press)
11. Kalazek, T.O., Olson, J.O., Irving, G.B., White, R. and Petrusso, R. An influenza outbreak due to A/USSR/77-like (H1N1) virus aboard a U.S. Naval Ship. (Manuscript in preparation)

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